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June 10, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Dear Sir or Madam:

RE: FOREIGN ESTABLISHMENT REGISTRATION AND LISTING
[DOCKET NO. 98N-1215]

This comment is directed to the proposed rule requiring foreign manufacturers to drug list every product intended for import into the United States for commercial distribution. The comment also addresses the information collection requirement under the Paperwork Reduction Act of 1995.

DRUG LISTING REQUIREMENTS FOR FOREIGN ESTABLISHMENTS

In the description of the proposed rule in the May 14, 1999 Federal Register, FDA states that the changes in Part 207 of Title 21 CFR make it mandatory that the foreign establishment drug list each product it exports to the United States for commercial distribution. The drug listing provisions actually do not change the original implementing regulations, which clearly required all drug products in commercial distribution in the United States to be listed regardless of source. However, the FDA description of the Part 207 requirements gives no recognition of the effect of 21 CFR 207.20(b) which is unchanged by the FDAMA law or the proposed revisions of implementing regulations. The FDA should recognize in its commentaries and implementation, that own label distributors may drug list the products they distribute in the U.S., and products that are drug listed by the distributor in accord with 21 CFR 207.20(b) are not required to be listed by the manufacturing establishment, whether domestic or foreign.

The Drug Listing Act of 1972 and the FDA implementing regulations were not intended to require a dual listing of drug information by the manufacturer, when the same information is supplied by the distributor. The 21 CFR Part 207 implementing regulations were adopted in 1973 with the FDA Commissioner's express declaration that "to avoid duplicity in the submission of drug listing information, registered establishments are not required to submit drug listing information for those products for which the distributor has submitted this information directly to the Food and Drug Administration."*[Federal Register, Vol. 38, No. 44, March 7, 1973, p. 6259,* copy enclosed.]

This was the FDA and industry standard and practice for over 20 years after the Drug Listing Act became law and the original implementing regulations were adopted. Within the last five years, however, FDA's Product Information Management Branch has demanded additional drug listing by the manufacturer of products already listed by the distributor, contrary to the 1972 law and implementing regulations.

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In addition to the plain words of the FDA Commissioner in 1973 stating the effect of the implementing regulations, the requirements of 21 CFR 207.20(b) make sense only if the distributor alone submits the drug listing information for a product, for these reasons:

1. It is elective and not mandatory for the distributor to submit the drug listing information, as the alternative choice to submission of the information by the manufacturer. There is no reason for the distributor to provide information if the manufacturer must separately list every drug.

2. The distributor must list the registration number of the manufacturer on Form FDA-2656, identifying the manufacturing facility to FDA. This requirement was intended to provide the information for the registered facility to FDA. If the registered facility independently listed each drug, there would be no need for the distributor to supply the information again.

3. "All distributors who submit drug listing information to FDA assume full responsibility for compliance with all the requirements of this part." This requires the drug listing distributor to assume the full responsibility for all of Part 207, including the drug listing obligations of the manufacturer under 21 CFR 207.21 (a) and (b).

4. "If the distributor does not elect to submit drug listing information directly to FDA and to obtain a Labeler Code, the registered establishment [manufacturer] shall submit the drug listing information."

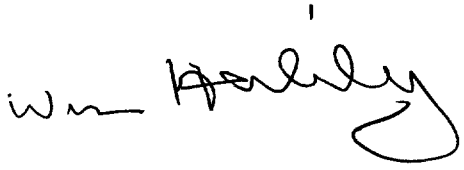
These last two provisions of the regulation make no sense if the manufacturer has a separate and unrelated duty to list each drug product, whether or not listed by the distributor.

If a separate drug listing by the manufacturer is necessary for a regulatory function that is not now served by the distributor's identification of the registered manufacturer on the FDA 2656 report, it is the obligation of FDA to publish a proposed amendment for comment and rulemaking. It would be a substantive change of the implementing regulations to require the mandatory submission of all drug listing information by the manufacturer whether foreign or domestic, where the distributor has provided the drug listing in compliance with 21 CFR 207.20(b).

INFORMATION COLLECTION REQUIREMENTS

Under the Paperwork Reduction Act of 1995, the requirement for dual listing by the registered manufacturing establishment whether domestic or foreign, is not necessary for the proper performance of FDA's functions, and the additional listing has no practical utility. FDA has all the information needed to identify drug manufacturers in the FDA-2656 submissions provided by distributors listing under Part 207.20(b). Adding a listing on the part of each drug manufacturing and processing facility only duplicates the drug listing information already known to FDA which would be repetitive, wasteful to the regulated industry, and ultimately more costly to consumers. A requirement for additional drug listings for the same product is contrary to the President's mandate to eliminate unnecessary regulations and relieve paperwork burden wherever possible.

Very truly yours,



William F. Herlihy
Associate General Counsel

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Enclosures

Title 21—Food and Drugs

CHAPTER I—FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

SUBCHAPTER C—DRUGS

PART 130—NEW DRUGS

PART 132—REGISTRATION OF PRODUCERS OF DRUGS AND LISTING OF DRUGS IN COMMERCIAL DISTRIBUTION

Establishment of Implementing Regulations for the Drug Listing Act of 1972

In the FEDERAL REGISTER of December 12, 1972 (37 FR 26431), the Commissioner of Food and Drugs proposed to amend 21 CFR Parts 130 and 132 to provide procedural regulations for the enforcement of the "Drug Listing Act of 1972," an Act to amend the Federal Food, Drug, and Cosmetic Act, which became effective on February 1, 1973. Interested persons were invited to submit comments on the proposal within 40 days. Comments were received from six trade associations and 18 manufacturers. In addition, members of the industry met with representatives of the Food and Drug Administration to discuss a means of achieving compatibility between the National Drug Code (NDC) and the Universal Product Code (UPC), a retail industry identification number.

The principal comments received and the Commissioner's conclusions are as follows:

1. Three drug manufacturers and one trade association objected to the statement in the preamble that the first listing of drugs will be required during June 1973. These persons state that the Drug Listing Act and the legislative history clearly reflect a congressional mandate that the first listing of drugs would not be required until the time of the first registration under section 510 of the Federal Food, Drug, and Cosmetic Act which occurs after the effective date of the Drug Listing Act. They noted that subsection 510(b) requires such registration on or before December 31 of each year. Accordingly, they believe that persons subject to the new drug listing requirements should not be required to submit drug listings prior to registration in December 1973.

The Commissioner does not agree with these comments. All persons who are registered are required under section 510(j)(2) to provide drug listing information once during the month of June of each year and once during the month of December of each year. Thus, for persons who are registered prior to February 1, 1973, the first drug list must be reported during the month of June 1973. In enacting the Drug Listing Act of 1972, Congress intended to provide the Food and Drug Administration with the legislative authority to compile a list of currently marketed drugs in order to assist the Agency in the enforcement of Federal laws requiring that drugs be safe and effective, and not adulterated or misbranded. In light of this congressional intent to protect the public health, the Comissioner can find no justification for delaying the filing of the first drug listing information beyond June 1973.

The Commissioner wishes to make clear that the filing of the drug list is separate from registration. Persons already registered are not required to "re-register" during June 1973. Persons who register under subsection 510 (c) or (d) between February 1 and June 1, 1973, are required under section 510(j)(1) to file the drug listing information at the time of registration. However, because of the time needed by the Food and Drug Administration to develop procedures for handling this information and for informing the affected industry as to how this information is to be reported, the Commissioner has determined that persons who register under § 510 (c) or (d) between February 1 and June 1, 1973, will not be required to submit the drug listing information until June 1973.

2. Four manufacturers of in vitro diagnostic products objected to the request that they register and submit drug listing information. The objections were based primarily on the contention that in vitro diagnostic products differ in many ways from conventional drug products and these differences make the proposed regulations inappropriate for such products. They further contend that many of these products are devices and therefore not subject to the drug registration and listing provisions of the Act.

In vitro diagnostic products that are drugs are clearly subject to all of the drug provisions of the Act, including the provisions of section 510. In vitro diagnostic products which are determined to be devices are not subject to section 510 of the Act and are therefore not subject to registration and listing. In any doubtful cases, the courts have held that the Food and Drug Administration has the legal authority to classify such products as drugs. Rather than attempt to classify all such products as drugs or devices, the Commissioner has proposed to establish a new procedure containing labeling requirements and a mechanism for establishing standards governing these products (37 FR 16613). The Food and Drug Administration is seeking the cooperation of the industry to register and submit drug listing in order to eliminate the need for regulatory action to obtain the information.

The Food and Drug Administration has the authority administratively to determine whether products are drugs or devices. Until new device legislation is enacted, and where the authority inherent in section 505 of the Act is necessary to adequately protect the public health, products which may be devices in the classic sense will be regarded as new drugs. No such determination will be necessary for listing purposes provided that the manufacturers of all in vitro diagnostic products register and submit the listing information.

Two manufacturers of in vitro diagnostic products requested that the Food and Drug Administration allow such manufacturers until December 1973 to submit listing information. The basis for this request is that most manufacturers of in vitro diagnostic products did not participate in the voluntary drug inventory program and will therefore require more time to develop listing information. The Commissioner has considered this request and has concluded that a June 1973 reporting date should allow ample time for the submission of listing information.

3. One manufacturer, while acknowledging that the preamble to the proposed regulations recognizes that they duplicate, in some respects, existing reporting requirements under sections 505, 507, and 512 of the Federal Food, Drug, and Cosmetic Act and section 351 of the Public Health Service Act, urged that steps be taken to eliminate such duplication in the final regulations. The Commissioner, although recognizing the problems associated with the duplicity of many of the reporting requirements, has concluded that it would be premature to eliminate or reduce this duplicity until the procedures of the drug listing regulations become fully operational. The Commissioner has determined that Congress, in enacting the Drug Listing Act, was aware that some of the information required to be submitted in the drug listing is required to be submitted to the Food and Drug Administration under existing regulations. However, Congress clearly intended that procedures be established for compiling the information required by the Drug Listing Act in a single system. As was stated in the preamble to the proposal, when the drug listing regulations become fully operative, steps will be undertaken to relieve the duplication, but such steps will still be compatible with the need for ready availability of the information for review purposes.

4. Two manufacturers submitted comments concerning the definition of "establishment" in § 132.1(a). One manufacturer requested that clinical chemistry laboratories be exempted from that part of the definition regarding "independent laboratories that engage in control activities for registered establishments (e.g., consulting laboratories)." This manufacturer expressed concern that such laboratories will no longer be willing to perform such services if they are required to register. The manufacturer also stated that the particular laboratory used by a manufacturer is generally proprietary information and that, if the Commissioner feels it to be essential that he be aware of these clinical laboratories, the manufacturer should submit the names of those he is using as a separate part of his drug listing information.

The Commissioner rejects the request that consulting laboratories not be required to register. The definition of "establishment" in the proposed regulations remains unchanged from that in the current regulations (21 CFR 132.1(b)) and consulting laboratories are already required to register. Such consulting laboratories are required to register in-

dependently of the firm for whom they perform services. Establishments who utilize the services of these consulting laboratories are not required to identify such laboratories in either their registration or drug listing submission. However, this does not exempt establishments from providing this information to the Food and Drug Administration when specifically requested.

A manufacturer stated that, since the proposed regulations can have no applicability to foreign establishments not registered under the Act, the definition of the term establishment should be amended to include only establishments registered under the Act. The Commissioner disagrees with this statement and sees no need to amend the definition of establishment as suggested by this manufacturer. The definition neither requires nor prohibits registration of foreign establishments. However, the 1972 law clearly requires a foreign drug manufacturer to comply with the drug listing requirements of the Act, whether or not he is registered. No unlisted drug may be imported into the United States. The proposed regulations contain no requirements regarding the registration of foreign establishments. The Commissioner published in the FEDERAL REGISTER of May 24, 1972 (37 FR 10510), a proposal concerning the registration of foreign drug establishments and a final order in this regard will be issued at a later date.

5. One manufacturer urged that the definition of "commercial distribution" in § 132.1(d) be revised so as to exclude products which are merely being distributed by a drug manufacturer. This manufacturer commented that section 510(j) of the Act requires the submission of drug listing information only for those drugs which the establishment manufactures, prepares, propagates, compounds, or processes. In addition, the manufacturer stated that if establishments include in their listing drugs which they merely distribute, the Food and Drug Administration will receive a false count as to the number of drugs actually being manufactured in this country.

The Commissioner has considered these comments but, in view of revisions of § 132.2 in the final regulations as to who must register and submit a drug list, has concluded that no revision in the definition of commercial distribution is necessary. Firms that merely distribute drug products and do not meet the definition of "manufacture, preparation, propagation, compounding, or processing" of a drug in § 132.1(c) are not required to register. In the final regulations a new § 132.2(b) is added to allow distributors (who are otherwise exempted from registration) to furnish drug listing information directly to the Food and Drug Administration for those products which they distribute under their own label but which are manufactured, prepared, propagated, compounded, processed, repackaged or otherwise changed in regard to container, wrapper, or labeling by a registered establishment. In such an instance, the Food and Drug Administration will assign a "Labeler Code" to the distributor and transmit drug listing instructions. To avoid duplicity in the submission of drug listing information, registered establishments are not required to submit drug listing information for those products for which the distributor has submitted this information directly to the Food and Drug Administration. This procedure is covered in paragraph 12(b) of this preamble.

6. Two trade associations and six manufacturers filed comments concerning the definition of "any material change" in § 132.1(g). In general, these comments suggested that the definition be revised to clarify that only "material or significant" changes in the labeling of a prescription drug or in the label or package insert of an over-the-counter drug are to be reported. In response to these comments, the applicable phrase of the definition of "any material change" has been revised in the final regulation to read "any significant change in the labeling of a prescription drug, and any significant change in the label or package insert of an over-the-counter drug." Changes that are not significant include changes in arrangement or printing or changes of an editorial nature.

7. One trade association submitted comments regarding the definition of bulk drug substance in § 132.1(h). The trade association said that it is not the intent of the Federal Food, Drug, and Cosmetic Act to require noncommercial in-house or subsidiary transfer of bulk drugs to conform to the requirements of the Drug Listing Act. They recommended that in order to exclude domestic and foreign internal transfers of bulk drug substances from the drug listing requirements, the phrase "or internal transfers of bulk drug substances" should be added to the end of the last sentence in § 132.1 (h).

The Commissioner agrees that it was not intended that owners or operators of registered establishments report as a separate entity on the drug list a bulk drug substance which is manufactured, prepared, propagated, compounded, or processed at one registered domestic establishment for noncommercial internal or interplant transfer for additional processing to another registered domestic establishment within the same parent, subsidiary, and/or affiliate company. However, because of the need to obtain and compile information on all drugs (bulk as well as finished dosage forms) which are imported into the United States and the requirements as set forth in § 132.31 that no drug may be imported into the United States unless it is first the subject of a drug listing, the proceeding statement concerning internal or interplant transfers of a bulk drug substance does not apply to such transfers between foreign and domestic establishments regardless if these establishments are within the same parent, subsidiary, and/or affiliate company.

Therefore the definition of "Commercial distribution" (§ 132.1(d)) is revised by adding the following phrase "but does not include internal or interplant transfer of a bulk drug substance between registered domestic establishments within the same parent, subsidiary, and/or affiliate company."

8. Four trade associations and one manufacturer offered comments regarding who must register and submit a drug list (§ 132.2). One trade association stated that a corporate group should be permitted to designate a single corporate member as the central registrant, regardless of so-called "parent" or "subsidiary" relationship, so long as there exists joint ownership and control among all the companies and suggested that the parenthetical clauses in § 132.2(a) be expanded to read "(except * * * parent, subsidiary and/or affiliate companies)." This same trade association also commented that the Food and Drug Administration should emphasize in the final order that establishments operating in intrastate commerce (including those marketing virus, serum, toxin, or analogous products for treatment of domestic animals in intrastate commerce) are required to register their establishments and list their products. One trade association suggested that the phrase "a list of drugs used" be used in place of the phrase "drug listing" in that part of the last sentence in § 132.2(a) relating to the manufacturing, preparation, propagation, compounding, or processing of an animal feed bearing or containing an animal drug. Another trade association stated that when the registration requirements contained in § 132.2 are viewed in context with the information required in registration and drug listings as set forth in § 132.5, it could be required that an "NDC" number be assigned when a new drug application (NDA) is initially submitted. This trade association suggested that the proposal be revised to require an "NDC" number assignment only when finished labeling for an approved NDA is submitted. One manufacturer submitted a similar comment remarking that, because of the long time span between submission of a new drug application, new animal drug application, antibiotic Forms 5 or 6, or Form 1800 (Medicated Feed Application) and FDA approval thereof, filings under this regulation should be deferred until submission of final printed labeling or some other act occurring late in the pendency of the application. One trade association suggested that intermediate premixes, feed additive concentrates, and feed additive supplements be exempt from drug listing along with medicated feeds.

The Commissioner agrees that a corporate group should be permitted to submit listing information for all subsidiaries and or affiliate companies when operations are conducted at more than one establishment so long as there exists joint ownership and control among all the establishments. However, each establishment must be registered separately. This is what was intended in the proposal. To clarify this intent, the parenthetical clauses in § 132.2(a) have been expanded in the final order to read "(except * * * parent, subsidiary and or af-

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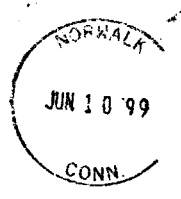

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